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Outcomes Res. & Evidence Based Med.

Principal Investigator: Biglan, Kevin M
Grant Number: 2L30NS050062-02
Title: Clinically Meaningful Outcomes in Parkinson's Disease

Abstract: Unavailable

Principal Investigator: BONATO, PAOLO
Grant Number: 5R21NS045410-02
Title: Data Mining to Identify Motor Fluctuations in PD

Abstract: The purpose of this project is to develop data mining and artificial intelligence systems to recognize the presence and severity of motor fluctuations in patients with Parkinson's disease (PD). Such a system would be valuable both for the clinical management of patients as well as for the conduct of trials of new treatments for PD. We hypothesize that movement disorders that accompany late-stage PD will present with identifiable and predictable features that can be derived from surface electromyographic (EMG) and accelerometer (ACC) signals recorded during the execution of a standardized set of motor assessment tasks. In the first phase of the project (R21) we will explore motor patterns associated with motor states (OFF, ON, DYSKINETIC). We will design methods that rely on data mining visualization techniques and vector quantization-projection algorithms for the identification of data clusters. Successful accomplishment of this exploratory phase will be followed by an R33 Phase in which we will develop a neuro-fuzzy system to provide clinical scores from automated analysis of the EMG and ACC features. Furthermore, we will perform a thorough analysis of motor pattems expressing the full complement of movement disorders associated with PD using fuzzy ARTMAP techniques. The approach will enable us to integrate clinical information into the quantitative EMG/ACC data analysis for the purpose of increasing our ability to identify the motor patterns associated with these disorders. Finally, Parkinsonian patients with motor fluctuations will be monitored before and after adjustment of their medications to assess the sensitivity of the technique to changes in the motor fluctuation patterns. Although this project focuses on a specific clinical application requiring advanced analysis techniques, the approach can be generalized to numerous applications in which data mining and other methods developed in this project can be used to analyze large data sets recorded using wearable sensors.-

Principal Investigator: Corcos, Daniel M
Grant Number: 5R01NS040902-05
Title: STN STIMULATION--NEURAL CONTROL OF MOVEMENT AND POSTURE

Abstract: High frequency stimulation of the subthalamic nucleus (STN) dramatically improves all of the clinical motor symptoms of Parkinson's Disease (PD). However, there are limited objective data available to determine which characteristics of movement and posture are affected by STN stimulation, and by what neural mechanisms this is accomplished. The long-term objective of this application is to obtain objective neurophysiological data relating to the mechanisms by which effective STN stimulation alters the spatial and temporal patterns of activity mediating planned movement and posture in humans. Patients in whom STN surgery is successful, as defined by a 30% reduction in the motor score of the Unified Parkinson's Disease Rating Scale, will take part in a series of experiments designed to investigate the neural control of movement and posture. The experiments in Aim I will use electromyographic (EMG) and motion analysis techniques to identify which aspects of strength, movement and standing balance are improved, worsened or unchanged by STN stimulation. The effects of STN stimulation will also be compared with the effects of medication on the control of strength and movement. The hypothesis is that neither STN stimulation nor medication normalizes the control of movement, and STN stimulation does not normalize the control of standing balance. Aim 2 will use electroencephalographic (EEG) techniques to test whether STN stimulation-induced changes in movement and gait initiation are accompanied by changes in the spatial and temporal patterns of cortical activity in response to both internally and externally generated cues to move. The hypothesis is that STN stimulation does not normalize the pathways that are normally influenced by the STN but does allow other pathways to compensate better. Aim 3 will combine EEG techniques with stimulation through the quadripolar electrodes implanted in the region of the STN to examine the pathways activated by effective STN stimulation. The findings of the proposed experiments will advance our understanding of the role of the STN in motor function, assist in the development of improved models of the role of the basal ganglia in the control of movement and posture, and thereby contribute to improved treatments for Parkinson's disease. -

Principal Investigator: Dambrosia, James
Grant Number: 5Z01NS002652-20
Title: Statistical Collaboration And Research

Abstract: Unavailable

Principal Investigator: ELSINGER, CATHERINE L
Grant Number: 1R43NS049705-01
Title: fMRI Evaluation of Parkinson's Disease

Abstract: Parkinson's disease (PD) is a progressive and incurable neurological disease affecting an estimated 4 million people worldwide. Health care costs in the U.S. alone have been estimated in excess of $6B. While many FDA-approved therapeutic interventions (pharmaceutical, surgical and physiological) have become available for the management of the motor and cognitive complications associated with PD, the majority of interventions become less effective over time as the disease progresses. The challenge is to develop more effective and longer lasting treatments that alter the disease course in addition to managing symptoms. Identifying incremental therapeutic efficacy over existing treatments may be hindered by existing clinical outcome measures that suffer from relatively low reliability and sensitivity. The next wave of clinical trials, therefore, will likely require reliable and sensitive biological markers that correlate with clinical outcomes. In Phase I of this project, we propose to test the efficacy of functional magnetic resonance imaging (fMRI), as a biomarker for quantifying a therapeutic response in PD. Phase II will entail the development of a standardized neuroimaging platform based on proprietary technology to be implemented across wide range of MRI scanner platforms. This commercial platform will target academic medical centers, hospitals, and clinics, as well as the pharmaceutical industry, in order to facilitate the evaluation of therapeutic response in PD. -

Principal Investigator: HOLLOWAY, ROBERT G
Grant Number: 5K24NS042098-04
Title: Neurology Outcomes Research:Clinical Trials/ Training

Abstract: New insights into the pathogenesis of Parkinson's disease (PD), the availability of a wider array of anti-parkinsonian therapies, the evolution of better tools for evaluating and monitoring disease progression have combined to change the current management of PD and the future landscape of PDrelated therapeutic clinical trials. This proposal outlines the key initial steps to develop the clinical trial methodology that allows for the longterm assessment of quality of life and economic outcomes in chronic neurological conditions. This will be accomplished by extending the duration of large multicenter clinical trial of pramipexole versus levodopa in early PD and augmenting the data collection effort to include clinical, quality of life, economic, and functional imaging outcomes. This will address questions for patients and providers on the best approach to treating early PD, as well as to provide a multidisciplinary research platform (clinical trials, quality of life assessment, and economic evaluation) to train a growing number of physician faculty and fellows at the University of Rochester in the theoretical, methodological, and practical knowledge and skills for a productive career in patient-oriented research. Dr. Holloway's position within the Departments of Neurology and Community and Preventive Medicine, and the Rochester Clinical Research Curriculum will ensure the recruitment of highly qualified trainees. -

Principal Investigator: KIEBURTZ, KARL D.
Grant Number: 5U01NS043128-04
Title: Neuroprotection Studies in PD: A Coordinating Center

Abstract: Unavailable

Principal Investigator: LANGE, NICHOLAS T
Grant Number: 2R01NS037483-06A1
Title: Biostatistical Methods for Human Brain Mapping

Abstract: This is a continuing proposal to address a variety of biostatistical problems motivated by current issues in imaging neuroscience, as during the previous funding cycle. New aims: the development of flexible semiparametric growth curve models for accelerated longitudinal designs; advancing methodology for replicated spatial point processes and 3-D brain brain cell assemblies; and new methods and algorithms for semiautomatic identification of human brain cells. We propose to generalize our proposed individual low-rank smooth regression methods to compositional data via a logit-Gaussian model within a hierarchical Bayes framework. We seek to produce practical guidelines for designing cost-effective longitudinal studies involving expensive outcomes measurements. We propose to advance Poisson random field methods for sparse processes, motivated by the multiple cell types and regional structures in the human brain. Empirical data analysis will continue to play a central role in the proposed research. Our human brain mapping research by magnetic resonance imaging (MRI) and positron emission tomography (PET) and human brain tissue microscopy again relates directly to the study of psychiatric and neurological outcomes in healthy and ill subjects, both young and old. Through our collaborating biostatistical and neuroscience institutions, our ongoing translational research develops and links modem biostatistical methods with complementary work in longitudinal anatomic human brain imaging, functional human brain imaging and human brain tissue microscopy. Brain diseases addressed are schizophrenia, bipolar disorder and Parkinson's disease. However, potential applications of our methods go well beyond human brain mapping to include longitudinal and spatial epidemiology, risk assessment, health policy and management, nutrition, and other fields in which cost and feasibility constraints impose restrictions on the numbers of subjects studied and on the numbers and timings of their repeated measurements.-

Principal Investigator: Oldfield, Edward
Grant Number: 5Z01NS002813-15
Title: Drug Delivery Techniques

Abstract: Unavailable

Principal Investigator: RICHARD, IRENE H
Grant Number: 5K23NS002184-05
Title: MOOD FLUCTUATIONS IN PARKINSON'S DISEASE

Abstract: The candidate has a clinical background in neurology with an expertise in movement disorders and has completed a two year NIH-funded fellowship through the Department of Neurology in Experimental Therapeutics. This fellowship provided the candidate with both theoretical knowledge and practical experience pertaining to the design and conduct of clinical trials. She has focussed most of her efforts thus far on the understanding and treatment of the behavioral aspects of Parkinson's disease (PD) The candidate's short term goals include the following: 1) to increase her knowledge of basic pharmacology and gain experience using techniques relevant to pharmacologic mechanism oriented research, 2) to gain a better understanding of molecular medicine, 3) to obtain training in psychiatric assessment techniques, 4) to expand her knowledge of areas fundamental to clinical investigation including biostatistics, epidemiology and outcomes research. The focus of her research plan during this career development award will be understanding mood fluctuations in PD. Mood fluctuations have been reported in up to 2/3 of advanced PD patients who experience motor fluctuations. These can be frequent, dramatic and distressing. Research involving the phenomenology and underlying mechanisms of mood fluctuations in PD has been limited. The specific aims of this study are to: 1) better understand the phenomenology of mood fluctuations in PD (frequency, quality, magnitude), 2) better understand the relationship between mood fluctuations and more pervasive depressive disorders in PD, 3) clarify the temporal relationship between changes in mood and motor states in PD, 4) elucidate the neurobiological mechanisms of changing mood states in PD and to determine, in particular, whether mood fluctuations in PD are the result of dopamine dysregulation, and 5) gather preliminary information regarding the optimal treatment of mood disorders in PD. These findings may lead to the development of therapeutic interventions for patients with PD who suffer from these disabling fluctuations on a daily basis. It may also provide a better understanding of the mechanisms responsible for more pervasive forms of depression in PD, and perhaps even in primary psychiatric mood disturbances. -

Principal Investigator: RICHARD, IRENE H
Grant Number: 1R01NS046487-01A1
Title: Study of Antidepressants in Parkinson's Disease (SAD PD)

Abstract: Depression is common in patients with Parkinson's Disease (PD), and is a major factor negatively impacting quality-of-life. To date, there have been no well-designed clinical trials of anti-depressant pharmacotherapy for depression in PD. Selective Serotonin Reuptake Inhibitor (SSRI) and, more recently, combined Serotonin and Norepinephrine Reuptake Inhibitor (SNRI) anti-depressants are used as a first-line treatment for depression. However, their efficacy and tolerability in PD have not been established, and there are several important reasons why results from studies in primary psychiatric populations cannot simply be extrapolated to patients with PD. In PD, the underlying pathophysiology and somewhat atypical depressive features may result in a different anti-depressant response. Furthermore, PD patients are particularly vulnerable to antidepressant-induced extrapyramidal side effects, and a host of factors (including concomitant anti-Parkinsonian medications) may affect the general tolerability of these agents. The proposed clinical trial has been designed to compare the efficacy and tolerability of Paroxetine (an SSRI) and Venlafaxine (an SNRI) in PD patients with depression. Information regarding the effects of these medications on motor function, quality-of-life, and cognition will also be obtained. Two-hundred, twenty-eight subjects will be enrolled among 15 centers, and each subject will participate in the trial for 12 weeks. The trial will clarify many important questions regarding the treatment of depression in patients with PD. -

Principal Investigator: SCHNEIDER, JAY S
Grant Number: 2R01NS038681-06
Title: GM1 Ganglioside Effects on Parkinson's Disease

Abstract: Parkinson's disease (PD) is a slowly but relentlessly progressive neurodegenerative disorder resulting in a time-dependent worsening of clinical symptoms. No drug has yet been identified that definitively slows or stops the progression of PD or substantially forestalls the inevitable functional decline in PD patients. Thus, disease modifying drugs that can modify clinical progression, enhance repair of damaged neurons, remediate existing neuropathological deficits, restore or enhance function of residual parts of the dopamine (DA) system and/or activate compensatory mechanisms are sorely needed. GM1 ganglioside may be such a treatment. In vitro and in vivo studies have shown GM1 to rescue damaged DA neurons, stimulate survival and repair of DAergic neuron and sprouting of functional DAergic terminals, increase DA levels in the striatum and upregulate DA synthetic capacity of residual neurons. Preliminary clinical studies of GM1 in PD patients have shown clinical improvements in patients with short-term use of GM1 and minimal symptom progression in patients with 2 to 5 years of GM1 use with resumed progression of symptoms following discontinuation of long-term GM1 use. The specific aims of this research are: 1) Assess the clinical efficacy of GM1 and the relationship between clinical improvement and in vivo quantitation of the integrity of the striatal DAergic innervation (assessed by PET imaging of the dopamine transporter site) in patients with typical mild/moderate PD in a randomized double blind placebo-controlled clinical trial. Working hypothesis: GM1 ganglioside treatment will result in symptomatic improvements related to effects on damaged but viable DA neurons and this may be accomplished through sprouting of functional DAergic terminals in the striatum. 2) Assess the extent to which long-term (2 years) use of GM1 ganglioside may stabilize symptoms or slow symptom/disease progression in PD patients (using clinical evaluations and PET imaging of the dopamine transporter as a surrogate measure). Working hypothesis: Long-term GM1 use will stabilize symptoms or slow the progression of symptoms in PD patients and this may be accompanied by reduced loss of striatal DA terminals over time. -

Principal Investigator: TICKLE-DEGNEN, LINDA
Grant Number: 5R01NS048059-02
Title: Culture, Gender, and Health Care Stigma in Parkinsonism

Abstract: The overall goal of the proposed research is to understand the stigmatizing role of the movement disorder of Parkinson's disease (PD) in health care practitioners' assessment of patient psychological traits, in the patient-practitioner relationship, and in the development of intervention recommendations. The first specific aim of the research is to elucidate the consequences of the operation of movement stereotypes on practitioner impressions of and conclusions about patients with PD. The second specific aim is to document the interaction of expressive masking (the diminishment of normal movement) with gender and culture on stigma outcomes. The third specific aim is to determine the degree to which practitioner expertise moderates the stigmatizing role of expressive masking on practitioner perceptions of and conclusions about patients. The fourth specific aim is to evaluate the clinical utility of the findings from the perspective of expert practitioners. Twelve Taiwanese patients (6 females and 6 males) and 12 American patients (6 females and 6 males) will be videotaped during a standardized health care interview in their respective homelands. Within each group of 6 patients (gender crossed with culture), there will be 3 patients with high expressive masking and 3 patients with normal expressive movement. Excerpts from the resulting 24 tapes will be shown to expert and novice health care practitioners in Taiwan and the U.S. who will assess patients' social and mental competence and potential for entering into a successful therapeutic relationship. In addition, the practitioners will make quality-of-life intervention recommendations. The results of the study will be presented to expert practitioners, in focus groups, who will evaluate the clinical utility of the findings and make recommendations for interventions to reduce practitioners' stigma responses. It is anticipated that PD with expressive masking will be more stigmatizing than PD without masking, especially as demonstrated in outcomes for novice compared to expert practitioners. It is also anticipated that negative outcomes of masking will be greater for female than male and American than Taiwanese patients because of different norms associated with movement expression in these groups.-

Principal Investigator: Tilley, Barbara C
Grant Number: 5U01NS043127-04
Title: Parkinson's Disease Clinical Trial: Statistical Center

Abstract: Unavailable

Principal Investigator: TILLEY, BARBARA C.
Grant Number: 3U01NS043127-04S1
Title: Parkinson's Disease Clinical Trial: Statistical Center

Abstract: Unavailable